REMARKS

Status of the Claims

After entry of the complete listing of the claims provided above, the status of the claims in this application are as follows:

Claims now pending in this application include: Claims 1-40.

Claims now amended include: Claims 1, 2-4, 8, 13-15, 18-21, 22-24, 28, 35 and 38-40.

Claims canceled include: Claims 41-952.

Claims added include: Claims 953-954.

Claim Amendments

As indicated above, several claims have been amended. Independent claims 1 and 21 have each been amended to recite "[a] composition of matter that comprises a library of nucleic acid analytes, and an array of nucleic acids, wherein said library comprises diverse nucleic acid analytes which comprise (i) an inherent universal detection target (UDT) [in the case of claim 1, a non-inhererent UDT in the case of claim 21] comprising at least one conserved sequence present in said diverse nucleic acid analytes, and (ii) a universal detection element (UDE), said UDE being attached to said UDT, said nucleic acid analytes being hybridized to said array of nucleic acids, and said array of nucleic acids being fixed or immobilized to a solid support, wherein said UDE generates a signal indicating the presence or quantity of said diverse nucleic acid analytes by means of said attachment of said UDE to said UDT."

Thus, claims 1 and 21 have both been amended to recite *nucleic acid* analytes in several instances. Support for the term "nucleic acid analytes" is drawn variously from the specification. See, for example, page 42, third paragraph ("An analyte is a biological polymer or ligand that is isolated or derived from biological sources such as organs, tissues or cells, or non-biological sources by synthetic or

enzymatic means or processes. Examples of biological polymers can include but are not limited to *oligonucleotides, polynucleotides*, . . ."). See also page 58, first line ("(ii) a library of *nucleic acid analytes* which may contain the nucleic acids of interest sought to be detected or quantified; . . ."); and page 58, second paragraph ((ii) a library of *nucleic acid analytes* which may contain the nucleic acids of interest;").

Support for other changes to claims 1 and 21 is also based in the original specification. In the case of "the diverse nucleic acid analytes," the specification discloses beginning with the last paragraph on page 42, and continuing through the first paragraph on page 43:

> Universal Detection Targets (UDTs) are defined as common or ***conserved segments in diverse nucleic acids that are present in populations of nucleic acids*** in a sample and are capable of recognition by a corresponding binding partner. The UDTs may be intrinsic or they may be artificially incorporated into nucleic acids. Examples of inherent UDTs can comprise but not be limited to 3' poly A segments, 5' caps, secondary structures and consensus sequences. Examples of inherent consensus sequences that might find use in the present invention can comprise but not be limited to signal sites for poly A addition, splicing elements and multicopy repeats such as Alu sequences. UDTs may also be artificially incorporated into nucleic acids by addition to the original analyte nucleic acid or during synthesis of nucleic acids that might comprise sequences that are identical or complementary to the sequences of the original analytes. Artificially added UDTs may be labeled themselves or they may serve as binding partners. [emphasis added]

Lastly, other changes to claims 1 and 21 fall into the category of transpositional changes. For example, the universal detection target (UDT) and the

universal detection element (UDE) have been brought forward into both claims as positive recitations and elements for the diverse nucleic acid analytes in the library of nucleic acid analytes. Thus, in claim 1, the "library comprises *diverse nucleic acid analytes which comprise (i) an inherent universal detection target (UDT) comprising at least one conserved sequence present in said diverse nucleic acid analytes, and (ii) a universal detection element (UDE), . . .*"

Several dependent claims have also been amended as follows. To define the present invention more clearly, claims 2 and 22 have each been amended to recite "wherein said library of *nucleic acid* analytes is *isolated* from a biological source *comprising* organs, tissues or cells." The term "nucleic acid analytes" has been addressed in the preceding paragraph.[1] Largely in response to the indefiniteness rejection (September 8, 2004 Office Action, page 2), the term "derived" in claims 2 and 22 has been changed to *isolated*. Support for *isolated* is drawn variously from the specification. See, for example, page 42, third paragraph under DETAILED DESCRIPTION OF THE INVENTION ("An analyte is a biological polymer or ligand that is isolated or derived from biological sources such as organs, tissues or cells, or non-biological sources by synthetic or enzymatic means or processes").

Other claims have been amended to change Markush language to more conventionally acceptable claim language. For example, claim 3 now recites "wherein said *nucleic acid* anaytes *comprise* genomic DNA, episomal DNA, unspliced RNA, mRNA, rRNA, snRNA *or* a combination of any of the foregoing." Similar changes have been effected to dependent claims 4, 8, 13, 14, 15, 18, 19, 20, 23, 24, 28, 35, 38, 39 and 40.

Finally, with respect to changes to the claims, new claims 953 and 954 have been added. Both new claims recite "wherein said nucleic acid analytes comprise DNA or RNA copies of genomic DNA, episomal DNA, unspliced RNA, mRNA, rRNA,

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[1] The term "nucleic acid" in the context of analytes has also been inserted into claims 3 and 23.

snRNA or combinations thereof." Support for the subject matter of new claims 953 and 954 is drawn variously from the original specification. For example, in the last paragraph on page 43, it is disclosed:

> The present invention discloses the use of UDTs and UDEs for the purpose of array analysis. The present invention also discloses novel methods for incorporation of production centers into nucleic acid libraries that may be used in array analysis. These production centers may provide amplification of sequences that are identical or complementary to sequences in the original diverse nucleic acid analytes. The products derived from these production centers may be labeled themselves or UDTs may be incorporated for detection purposes. ***Nucleic acids that may be of use in the present invention can comprise or be derived from DNA or RNA. The original population of nucleic acids may comprise but not be limited to genomic DNA, unspliced RNA, mRNA, rRNA and snRNA.*** [emphasis added]

In addition, the specification discloses nucleic acid analyte copies in several instances. See, for example, page 53, lines 3-5 ("Other compositions of matter are provided by this invention. One such composition comprises a library of first *nucleic acid analyte copies*, such first nucleic acid copies being hybridized to an array of nucleic acids, those nucleic acids being fixed or immobilized to a solid support, . . .") [italics added]. See also same page, second full paragraph ("Another composition of matter comprises a library of first *nucleic acid analyte copies*, such first nucleic acid copies being hybridized to an array of nucleic acids, the nucleic acids being fixed or immobilized to a solid support, . . .") [italics added].

In view of the above-quoted portions in the specification, it is believed that the subject matter of new claims 953 and 954 is fully supported by Applicants' disclosure.

It is believed that no new matter has been inserted by any of the above amendments to the claims or the two newly added claims. Entry of the above amendments and new claims is respectfully requested.

Information Disclosure Statement Filed January 7, 2004

In the September 8, 2004 Office Action (page 2), the Examiner indicated that "[t]he documents 0104620 and 0104460 lined through in PTO-1449 filed 1/7/04 were not signed because the documents were not found." A review of Applicants' January 7, 2004 Information Disclosure Statement reveals that the documents in question are Rabbani et al., U.S. Patent Application Publication No. US 2003/0104620 A1, published on June 5, 2003; and Rabbani et al., U.S. Patent Application Serial No. 09/104,067, filed on June 24, 1998. The former is listed as Document No. 39 and the latter as Document 40. In order to complete the record and to ensure consideration by the Examiner, Applicants are providing copies of these documents. In the case of Document No. 39, a copy of US 2003/0104620 A1 is attached to this paper as Exhibit 1. With respect to Document No. 40, Applicants have attached copies of two U.S. patents that were issued earlier this year based upon the aforementioned priority document, Serial No. 09/104,067. The two U.S. patents are U.S. 6,743,605 B1, issued on June 1, 2004, and U.S. 6,764,821, issued on July 20, 2004. Copies of the '605 and '821 Patents are attached as Exhibits 2 and 3, respectively.

Applicants respectfully request that consideration be given to all three documents submitted herewith as Exhibits 1-3.

The Rejection Under 35 USC §112, Second Paragraph

Claim 2 stand rejected for indefiniteness under 35 U.S.C. §112, second paragraph. In the September 8, 2004 Office Action (page 2), the Examiner stated:

a. Claim 2 is vague and indefinite because of the phrase "derived from". Since the phrase "derived from" is used to describe a chemically modified compound, it is unclear whether or not the analyte from a biological source is chemically modified. Clarification is required.

As indicated above, claims 2 and 22 have been amended to recite that the library of *nucleic acid* analytes is *isolated* from a biological source. The deletion of the term "derived from" is believed to have obviated the grounds for the indefiniteness rejection.

In view of the above amendments to claims 2 and 22, Applicants respectfully request reconsideration and withdrawal of the indefiniteness rejection.

The Rejection Under 35 USC §102

Claims 1-4, 7, 11, 13-15, 17-24, 27, 33-35 and 37 stand rejected under 35 U.S.C. §102(e) as being anticipated by Li, U.S. Patent No. 6,696,256 B1. In the September 8, 2004 Office Action (page 3), the Examiner states:

> Li discloses that a hybridization array is for use in identifying a plurality of different activated transcription factors in a biological sample (See column 5, lines 4-21). The biological sample is derived from a sample of cells (See column 10, lines 52-55). The transcription factor probes are attached to different fluorescent dye (See column 17, lines 60-67). The method of Li et al. involves using a hybridization array to hybridize to the transcription factor probe (See column 19, line 7-16). The detectable marker can be chemiluminescent avidin or antibodies (See column 13, lines 50-67 and column 14, lines 1-9). Thus, each element used in the array of Li anticipates the limitations of claims as discussed above.

The anticipation rejection is respectfully traversed.

As indicated in the opening remarks of this paper, the present claims, notably independent claims 1 and 21, have been amended to recite "[a] composition of matter that comprises a library of nucleic acid analytes, and an array of nucleic acids, wherein said library comprises diverse nucleic acid analytes which comprise (i) an inherent universal detection target (UDT) [a non-inherent UDT in the case of claim 21] comprising at least one conserved sequence present in said diverse nucleic acid analytes, and (ii) a universal detection element (UDE), said UDE being attached to said UDT. The nucleic acid analytes are hybridized to the array of nucleic acids, and the array of nucleic acids are fixed or immobilized to a solid support. According to both claims 1 and 21, the UDE generates a signal indicating the presence or quantity of said diverse nucleic acid analytes by means of said attachment of said UDE to said UDT.

There are at least two material features in the present invention that are altogether lacking in Li's patent. First, Li discloses nucleic acids that quantify the amount of transcription factors analytes in a sample. In contrast to Li, the present invention provides labeled transcription factors [in the form of a UDE] that quantify analyte nucleic acids in a sample. Second, Li discloses a single nucleic acid sequence for any given transcription factor, whereas in the present invention, the claim UDT is a ***universal*** detection target that comprises ***at least one conserved sequence present*** in the ***diverse nucleic acid analytes***. Thus, in the present invention, when a variety of different [diverse] nucleic acid analytes are hybridized to an array of nucleic acids, signal generation can take place for a number of different nucleic acid analytes [each with their own unique sequences] by binding a labeled UDE to the shared UDT sequence.

In view of the lack of identity of material elements between the present invention and the cited Li patent, Applicants respectfully request reconsideration and withdrawal of the anticipation rejection.

The Rejection Under 35 USC §103

Claims 5-6, 8-10, 12, 16, 25-26, 28-32, and 36-40 stand rejected under 35 U.S.C 103(a) as being unpatentable over Li, U.S. Patent No. 6,696,256 B1, as applied to claims 1-4, 7, 11, 13-15, 17-24, 27, 33-35 and 37 above, and further in view of Kool et al., U.S. Patent No. 6,479,650 B1. In the September 8, 2004 Office Action (pages 4-5), the Examiner stated:

> The teachings of Li are set forth in section 4 above. Li does not disclose modified sugar or phosphate or base moieties, solid support and PNA.
>
> Kool et al. disclose a combinatorial flurophore array library comprising nucleoside analogs attached to one or more solid support (See the Abstract). The oligonucleotide analogs comprising one or more of the subject nucleoside analogs have a modification to the sugar-phosphate base and have peptide nucleic acid (PNA) (See column 4, lines 56-62). The solid supports include polyacrylamid or pore glass (See column 18, lines 61-67). There is a spacer molecule (It is considered to a linker or linker arm) between solid support and nucleoside analog (See column 19, lines 12-15).
>
> One of ordinary skill in the art would have been motivated to apply the modification to the sugar-phosphate base, PNA, the solid supports and the spacer molecule used as linker arm of Kool et al. to the array of Li. The motivation is that the array of Kool et al. is to be used in detecting a target nucleic acid in sample (See column 4, lines 3-9) and the nucleoside analog used in the array improves fluorescence characteristics, increasing the range of emission wavelengths in which it is useful in biophysical and diagnostics applications (See column 2,

line 1-3). It would have been prima facie obvious to apply the modification to the sugar-phosphate base, PNA, the solid supports and the spacer molecule used as linker arm of Kool et al. to make the composition comprising the library of analytes, and array of nucleic acid in which the nucleic acid is fixed on a solid support and the analytes comprise UDT and UDE.

The obviousness rejection is respectfully traversed.

As indicated above in the anticipation rejection, Li's disclosure lacks mention of at least two material elements from Applicants' claimed invention. The first material difference lies in Li's disclosure of an unlabeled protein [transcription factor] in conjunction with labeled nucleic acid, whereas the present invention is directed to labeled proteins [UDEs] in conjunction with unlabeled nucleic acid analytes [with UDTs]. The second material difference is reflected in the present claims that recite a universal detection target that comprises at least one conserved sequence present in the diverse nucleic acid analytes hybridized to the array of nucleic acid.

Even if one of ordinary skill in the art were sufficiently motivated to use Kool's elements in an attempt to modify Li's arrays, such a person would not reach the present invention because both Kool and Li only disclose labeled nucleic acids. Neither Kool nor Li describe labeled sequence-specific proteins as provided in the present invention.

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SUMMARY AND CONCLUSIONS

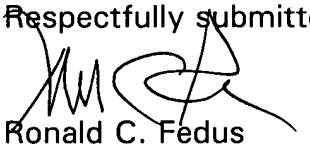
A complete listing of the claims in this application are provided above. In the complete listing of the claims, twenty claims (1, 2-4, 8, 13-15, 18-21, 22-24, 28, 35 and 38-40) have been amended and two new claims (953 and 954) have been added.

The fee for adding two new claims (953 and 954) is $18. The Patent and Trademark Office is herby authorized to charge the requisite $18 claim fee to Deposit Account No. 05-1135. No other fee or fees are believed due for this paper. In the event that any other fee or fees are due, however, authorization is hereby given to charge the amount of any such fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Early and favorable action is respectfully requested.

Respectfully submitted,



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